The NEW ENGLAND JOURNAL of MEDICINE

Insulin Efsitora versus Degludec in Type 2 Diabetes

A PLAIN LANGUAGE SUMMARY

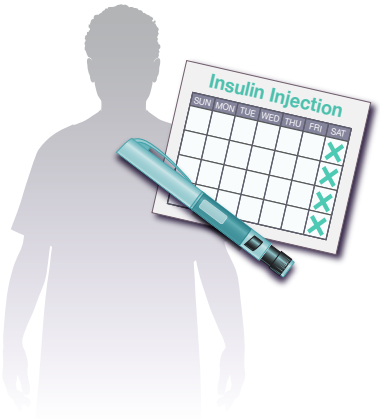
Based on the NEJM publication: Insulin Efsitora versus Degludec in Type 2 Diabetes without Previous Insulin Treatment by C. Wysham et al. (published September 10, 2024)

In this trial, researchers assessed the efficacy and safety of once-weekly insulin efsitora alfa as compared with once-daily insulin degludec, both in combination with noninsulin glucose-lowering agents, in adults with type 2 diabetes who had not previously received insulin.

As type 2 diabetes progresses, the timely addition of basal insulin to therapy is recommended when noninsulin glucose-lowering agents alone are not adequate to maintain glycemic control.

WHY WAS THE TRIAL DONE?

Daily insulin injections may be a burden for persons with type 2 diabetes. Insulin efsitora is a new basal insulin designed to have a flat pharmacokinetic profile and a long half-life, allowing for once-weekly administration. Findings from phase 2 trials comparing insulin efsitora with insulin degludec have been promising; additional data are needed.



HOW WAS THE TRIAL CONDUCTED?

Adults with type 2 diabetes who had not previously received insulin were assigned to receive subcutaneous insulin efsitora once weekly or subcutaneous insulin degludec once daily for 52 weeks, in addition to their usual glucose-lowering agents. The insulin dose was assessed weekly up to week 12 and every 4 weeks thereafter, with adjustments as needed to achieve a fasting blood glucose level of 80 to 120 mg/dl. The primary end point was the change in the glycated hemoglobin level from baseline to week 52; the noninferiority margin was 0.4 percentage points.

Insulin Efsitora Alfa
Once weekly for 52 weeks

466 Participants

Insulin Degludec
Once daily for 52 weeks

462 Participants

PARTICIPANTS

WHO

- 928 adults
- Mean age, 57 years
- Men: 59%; Women: 41%

CLINICAL STATUS

- Glycated hemoglobin level, 7.0 to 10.5%
- BMI, 45 or less
- Stable treatment with 1 to 3 noninsulin glucose-lowering agents for at least 3 months before screening
- No previous insulin therapy

TRIAL DESIGN

- PHASE 3
- OPEN-LABEL
- NONINFERIORITY
- RANDOMIZED
- CONTROLLED
- LOCATION: 121 SITES IN 10 COUNTRIES

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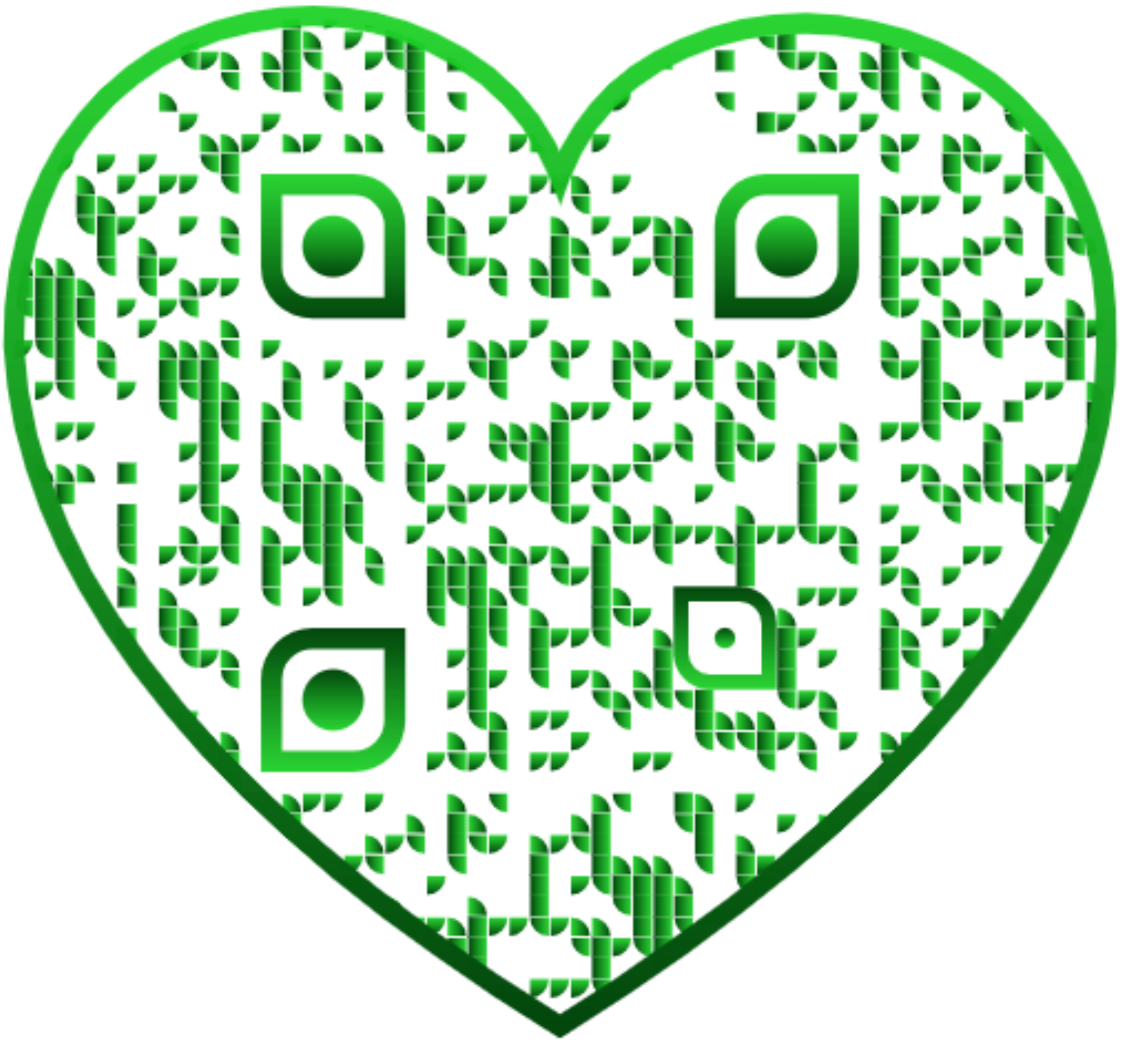
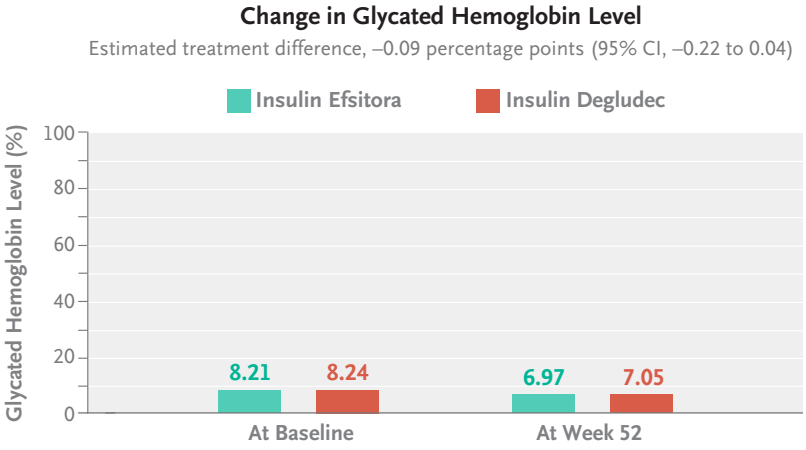
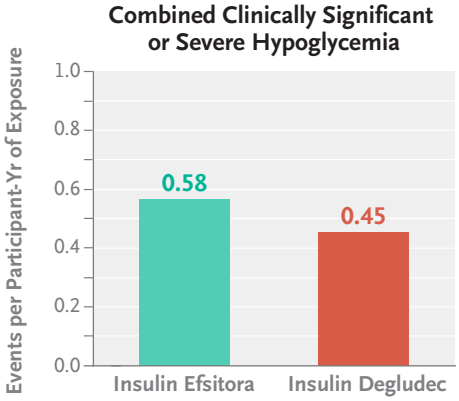


RESULTS

Insulin efsitora was found to be noninferior to insulin degludec with respect to the change in the mean glycated hemoglobin level from baseline to week 52.

Noninferiority was also shown in subgroups of participants using and not using glucagon-like peptide-1 receptor agonists.





The rate of combined clinically significant or severe hypoglycemia was similar in the two groups.

GLYCEMIC CONTROL

In both groups, a mean glycated hemoglobin level of less than 7% was attained after 16 weeks of treatment and sustained until the end of the treatment period.

LIMITATIONS AND REMAINING QUESTIONS

- The trial was open-label, which may have introduced bias.
- Participants wore a blinded continuous glucose monitoring device intermittently during the trial, which could not be used for dose adjustments. Use of the device for dose adjustments might have further improved glycemic control and reduced hypoglycemia.

CONCLUSIONS

In adults with type 2 diabetes who had not previously received insulin, once-weekly insulin efsitora was noninferior to once-daily insulin degludec in reducing glycated hemoglobin levels at 52 weeks.

LINKS: FULL ARTICLE | NEJM QUICK TAKE | EDITORIAL

FURTHER INFORMATION

Trial registration: ClinicalTrials.gov number, NCT05362058

Trial funding: Eli Lilly

Full citation: Wysham C, Bajaj HS, Del Prato S, et al. Insulin efsitora versus degludec in type 2 diabetes without previous insulin treatment. N Engl J Med 2024;391:2201-11. DOI: 10.1056/NEJMoa2403953

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